REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated May 20, 2002, the period for response to which will expire on August 20, 2002.

In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Claims 1-4 and 30-37 are under consideration in this application. Claims 7, 19, 20, 22 are being canceled without prejudice or disclaimer, and claims 1-4 and 30-32 are being amended, as set forth above and in the attached marked-up presentation of the claim amendments, in order to more particularly define and distinctly claim applicants' invention. New claims 33-37 are being added to recite other embodiments described in the specification. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

Prior Art Rejection

Claims 1-4, 7, 19-20, 22, and 30-32 were rejected under 35 U.S.C. § 103(a) as being unpatantable over WO 98/06872 (U.S. Pat. No. 6,007,231) to Vijg et al (hereinafter "Vijg") in view of an article by Xu et al (hereinafter "Xu"). The rejection has been carefully considered, but is most respectfully traversed.

The present invention is characterized in a primer design system that comprises means for selecting at least one genomic DNA nucleotide sequence from a database including a plurality of DNA nucleotide sequences; means for predicting a plurality of exons of said selected DNA nucleotide and for storing positions of the predicted exons; means for simultaneously designing a plurality of primer pairs by using each of the predicted exons as a template; and means for automatically collating said plurality of primer pairs with said predicted exons and the DNA nucleotide sequence.

The whole method of the present invention, including all steps in Fig. 10 and the transitions therebetween, is performed "automatically" contrary to the prior art that executes and links two or more steps "manually" so as to collate the pairs of primers with the positions on a plurality of genomic DNA nucleotide sequences. The invention first randomly divides each genomic DNA into fragments of various lengths then predicts exons in each fragment simultaneously. Each of a plurality of predicted exons are then used as templates to design primers. Alternatively, the information regarding I/E junctions is input from an externally database so as to design primers.

The designed primers are then selected with a condition of a base length 20-28 bps and at least one of the following conditions:

(a) with a GC content of 50-60%;

(b) with Tm = 50-80oC and $|\Delta Tm| < 20oC$;

(c) being located as close to the 5' end or the 3' end as possible;

(d) including non-specific at least one binding region, such as a loop structure.

Thereafter, each selected primer and primer set are evaluated with BLAST for specificity.

First of all, Applicants respectfully contend that neither Vijg nor Xu teaches or suggests simultaneously designing a plurality of primer pairs by using each of the predicted exons as a template. In contrast, Vijg only processes one exon at a time to design a primer pair (col. 14, lines 10-12). Rather than one exon, a plurality of exons 1-n are processed in parallel as shown in Fig. 21 according to the invention with plural CPUs working simultaneously so as to predict a primer pair from each exon.

Secondly, none of the cited references teaches or suggests randomly dividing at least one genomic DNA into fragments as templates for exon prediction. Vijg simply fails to discuss exon prediction. Xu was relied upon by to Examiner to compensate for Vijg's deficiency in this regard. However, Xu's approach is developed for identifying exon boundaries in a cDNA rather than a genomic DNA.

Thirdly, none of the cited references teaches or suggests evaluating each selected primer and primer pair for specificity. Vijg and Xu simply fail to mention any thing in this regard.

Fourthly, neither Vijg nor Xu teaches or suggests the primer selecting conditions (a)-(d). Xu simply fails to mention anything in this regard. As to Vijg, it mentioned something that appears to be similar but is in fact totally different. For example, Vijg applies a GC clamp rather than a GC content as in the invention. The nature and function of the GC clamp are totally different from that of the GC content of the invention according to the recitation in Vijg: "It is common practice to couple one of the two primers surrounding a gene target fragment to a GC-rich clamp sequence of about 30 bases pairs long. This clamp is very stable and functions as the highest melting domain; that is, the part of the DNA molecule that keeps the fragment together." (col. 2, lines 58-63). As another example, Vijg requires each pair of primers to have substantially the same annealing temp ($\pm$ 5°C, col. 5, line 60; col. 14, line 3). On the other hand, two different Tm conditions, i.e., Tm = 50-80°C and $|\Delta Tm| < 20°C$, are used to screen primers in the invention. (c) and (d) are simply absent from Vijg.

Lastly, the Examiner relied upon the combination of Vijg's teaching of automatically extracting exons of a genomic DNA(col. 11, line 42), and Xu's teaching of identifying exon boundaries of a cDNA to cover the features of the invention. However, no motivation was provided for one skilled in the art to combine the conflicting principles of operation in Vijg (**actual** exon prediction based upon a genomic DNA) and Xu (automatic **simulation** based upon a cDNA). On the contrary, the huge data amount incurred in an automatic primer design system based upon a genomic DNA discourages such a combination.

Even if, arguendo, a person of ordinary skill were motivated to combine the teachings in

Vijg and Xu, such combined teachings would still fall short in fully meeting the Applicants' claimed invention as set forth in claim 1 since, as discussed, there are no teachings of (1) simultaneously designing a plurality of primer pairs by using each of the predicted exons as a template, (2) randomly dividing at least one genomic DNA into fragments as templates for exon prediction, (3) evaluating each selected primer and primer pair for specificity, or (4) primer selecting conditions (a)-(d) in either Vijg or Xu.

It is respectfully submitted that the cited references do not teach or suggest each and every element of the applicants' invention as now set forth in other independent claims 1, 30 reciting the same novel feature. Accordingly, the withdrawal of the outstanding rejections under 35 U.S.C. §103 is in order, and is respectfully solicited.

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art references upon which the rejections in the Office Action rely, Applicants respectfully contend that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application as amended is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of the above-captioned application, the Examiner is invited to contact the Applicants' undersigned representative at the address and phone number indicated below.

Respectfully submitted,

Stanley P. Fisher
Registration Number 24,344

JUAN CARLOS A. MARQUEZ
Registration No. 34,072

REED SMITH LLP
3110 Fairview Park Drive
Suite 1400
Falls Church, Virginia 22042
(703) 641-4200

August 20, 2002

SPF/JCM/JT

Marked-up Version of Amended Claims

1. A primer design system, comprising:

means for selecting at least one genomic DNA nucleotide sequence from a database including a plurality of [different] DNA nucleotide sequences [of the human genome];

means for predicting a plurality of [different] exons of said selected DNA nucleotide and for storing positions of the predicted exons; [and

a control unit for controlling the system, said control unit controlling:]

means for [extracting] simultaneously designing a plurality of [partial sequences] primer pairs by using each of the predicted exons as a template; [meeting extraction conditions from the predicted exons, wherein said extraction conditions include a predetermined base length;

means for determining positions of said plurality of partial sequences related to each one of said predicted exons and the DNA nucleotide sequence;

means for selecting a plurality of different partial sequences from said plurality of partial sequences and based on results of said position determining means;

means for determining a plurality of pairs of primers for normal PCR for each of said plurality of different partial sequences;] and

means for automatically collating said plurality of primer pairs [of primers] with said predicted exons and the DNA nucleotide sequence.

2. A primer design system according to claim 1, [said control unit] further comprising [controls second] means for selecting a plurality of primer[s] pairs meeting certain selection conditions from [said plurality of partial sequences extracted by said extracting means] the designed primer pairs.

3. A primer design system according to claim 2, said selection conditions [determine] include at least one of a predetermined base length, [the] a range of GC content and[/or] a range of Tm [of DNA nucleotide sequences to be selected].

4. A primer design system according to claim 1, [said control unit] further comprising means for evaluating specificity of each designed primer or primer pair[controls means for limiting the plurality of mutually different DNA nucleotide sequences, the data for which were obtained by said selecting means, to a base length longer than said certain base length, to be output to said extracting means].

30. A method for designing primers, comprising the steps of:

selecting at least one DNA nucleotide sequence from a genomic DNA database[, said database including a DNA nucleotide sequence of the human genome];

predicting a plurality of exons of said selected DNA nucleotide [using at least

one exon predicting program];

simultaneously designing a plurality of primer pairs by using each of the predicted exons as a template; and

automatically collating said plurality of primer pairs with said predicted exons and the DNA nucleotide sequence [extracting a partial sequence corresponding to each of said predicted exons meeting extraction conditions, wherein said extraction conditions include a base length; and

determining the primers for each of said extracted partial sequences].

31. A method for designing primers according to claim 30, further comprising a step of selecting a plurality of primer pairs meeting certain selection conditions from said plurality of designed primer pairs, wherein said extraction conditions include [a condition selected from the group consisting of] at least one of a predetermined base length, a GC content[s], Tm[, Tm, and combination thereof].

32. A method for designing primers according to claim 30, further comprising a step of evaluating specificity of each designed primer or primer pair [the steps of: after said extracting step, selecting at least one partial sequence from said extracted partial sequences based on the results of a homology search that utilizes said extracted partial sequences as a query].